PATENT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant: Henslee et al.

Serial No.: 09/975,502

Filed: October 11, 2001

For: REAGENTS AND METHODS USEFUL FOR DETECTING DISEASES OF THE BREAST

Case No.: 5972.US.P7

Examiner: Harris, A.

Group Art Unit: 1643

I hereby certify that this paper (along with any paper referred to as being attached or enclosed) is being deposited with the United States Postal Service on the date shown below with sufficient postage as first class mail in an envelope addressed to the:

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Date of Deposit:

Kimberly A. Morris 1-31-06.
Date

DECLARATION

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Sir:

I, Dr. Barry Dowell, do hereby declare and state that:

I am a citizen of the United States of America and reside at 197 Knightsbridge Drive, Mundelein, Illinois 60060.

I graduated in 1972 from the University of North Carolina at Chapel Hill and received a B.S. degree in Zoology, and I graduated in 1977 from the University of Tennessee Center for the Health sciences and received a Ph.D. degree in Microbiology and Immunology (see the attached curriculum vitae).

I have been employed as a Manager, Cancer Core R&D, Abbott Diagnostics Division at Abbott Laboratories, Abbott Park, Illinois since 2004. I have been employed in several other positions at Abbott Laboratories since 1987.

I have read and am familiar with the specification and pending claims of U.S. Patent Application Serial No. 09/975,502. Furthermore, I have reviewed the Office Action of November 1, 2005 issued by the Examiner in the above-referenced application and have reviewed the prior art cited by the Examiner with respect to the obviousness rejection of claims 2-4.

In my opinion, one of ordinary skill in the art would not have been motivated to have created the subject matter of claims 2-4, at the time of filing of the application, based upon the teaching of U.S. Patent Application Publication No. 2002/0009738A1 (Houghton et al).

Houghton et al. describe the identification of tissue-specific polynucleotides and methods for determining the presence of cancer in a patient by detecting polynucleotides which encode breast tumor proteins.

The Examiner contends that it would have been *prima facie* obvious to one of ordinary skill in the art at the time the claimed invention was made to use antibodies via an immunoassay in the detection of the taught breast tumor proteins in a patient sample within a tissue section or cell culture, and that one would have been motivated to do so with a reasonable expectation of success by the

teachings of Houghton et al. to detect two breast tumor proteins. In particular, the Examiner notes that the publication discloses that "what is needed in the art is a methodology that employs the detection of two or more breast cancer specific genes in order to improve the sensitivity and reliability of detection of micrometastases". (Page 1, section 0009.) Thus, the Examiner concludes that it would follow that detection of encoded polypeptides would be useful in the diagnosis of breast cancer.

In my opinion, the Examiner is incorrect with respect to the conclusions made. It is certainly not obvious that because a gene is expressed, the encoded protein is automatically expressed as well as secreted. In fact, Houghton et al. do not even disclose expressed proteins whatsoever. It must be emphasized that all expressed polynucleotides do not result in increased expression of the respective encoded polypeptides for various reasons; thus, it would not have been obvious that measuring the polypeptide of interest would be useful from a diagnostic perspective. Further, the presence of two polynucleotides, for example, would not have rendered obvious, or motivated one of ordinary skill in the art, to predict the presence of the two encoded proteins of a specific combination. Moreover, the use of the separate antibodies to separately find each member of the combinations of specific polypeptides is certainly not obvious.

In view of the above, one of ordinary skill in this field would not have been motivated to have created the

subject matter of claims 2-4 based upon the teachings and suggestions of Houghton et al. Significant skill was required in connection with the subject matter of claims 2-4 of the above-referenced application.

I declare further that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the instant patent application or any patent issuing thereon.

Respectfully submitted,

By: Barry Dowell

Dr. Barry Dowell

Date: 12/15/05

RESUME

Barry Lee Dowell, Ph. D.

CURRENT POSITION

Associate Research Fellow, Volwiler Society
Manager, Cancer Core R&D

EDUCATION

1972	B. S. (Zoology), University of North Carolina at Chapel Hill
1977	Ph. D. (Microbiology and Immunology), University of Tennessee Center for the Health Sciences, Memphis
1977-1979	Postdoctoral Fellow (NRSA), Department of Microbiology and Immunology, Duke University, Durham, North Carolina

PROFESSIONAL ORGANIZATIONS

American Association for the Advancement of Science
American Association of Clinical Chemists
American Association of Immunologists
American Society for Microbiology
Clinical Ligand Assay Society

HONORS AND AWARDS

1980-1982	Special Fellow, Leukemia Society of America
1983-1984	Biomedical Research Support Grant
1985	Geometric Cell Labelling Grant
1986-1987	Ronald McDonald Children's Charities Grant
1989	Chairman's Award, Abbott Laboratories, IMx APF
1991	Chairman's Award, Abbott Laboratories, IMx PSA
1992	Abbott Diagnostics Division Technical Advisory Board, Entrepreneurial Award for IMx PSA Team
1992-Present	Associate Research Fellow, Volwiler Society
1993, 1994	Member and Presenter for First and Second Stanford Conference for the International Standardization of PSA
1993-1996	Full Member, PSA Standardization Subcommittee of National Committee for Clinical Laboratory Standards
1997	Abbott Diagnostics Division Technical Advisory Board, Technology Award for Free PSA Team
1997	Chariman's Award, AxSYM Free and Total PSA
1997	Member, Steering Committee, ISOBM TD-3 (PSA Antibody) Workshop
1998	Expert Reviewer for Urology
2000-2001	Two VP Awards for FDA Compliance Efforts (Conjugate Common Process)
2003-2004	Member of NACB Committee for Guidelines for Prostate Cancer Diagnosis

April 2003

PROFESSIONAL EMPLOYMENT

1972-1978	Microbiology Teaching Assistant, Department of Microbiology, University of Tennessee Center for Health Sciences, Memphis
1980-1981	Research Associate, Department of Microbiology and Immunology, Duke University, Durham, North Carolina
1981-1982	Medical Research Associate, Cancer Center Faculty, Department of Microbiology and Immunology, Duke University, Durham, North Carolina
1982-1987	Assistant Professor, Departments of Pediatrics and Microbiology and Immunology, Baylor College of Medicine, Houston, Texas
1987-1989	Project Manager for IMx APF, Biologist II, Cancer Product Development, Research and Development, Abbott Laboratories, Abbott Park, Illinois
1989-1991	Project Manager for IMx PSA, Senior Research Biochemist, Cancer Product Development, Research and Development, Abbott Laboratories, Abbott Park, Illinois
1991-1992	Group Leader for IMx CA15-3, IMx PAP, PSA Futures, Research Invest. Biochemist, Cancer Product Development, Research and Development, Abbott Laboratories, Abbott Park, Illinois
1992-1994	Group Leader for IMx CA15-3, IMx PAP, PSA Futures, Cancer Product Research and Development and Associate Research Fellow, Volwiler Society Abbott Laboratories, Abbott Park, Illinois
1995-1996	Lead Scientist for AxSYM Total PSA and AxSYM Free PSA, Cancer Product Research and Development and Associate Research Fellow, Volwiler Society Abbott Laboratories, Abbott Park, Illinois
1996-1998	Project Manager for AxSYM Total PSA and AxSYM Free PSA, Cancer Product Research and Development and Associate Research Fellow, Volwiler Society Abbott Laboratories, Abbott Park, Illinois June, 1996
1998-1999	R&D Manager, Diseases of Aging Venture Group and Associate Research Fellow, Volwiler Society Abbott Laboratories, Abbott Park, Illinois
1999-2000	R&D Manager, Breast Cancer Venture Group and Associate Research Fellow, Volwiler Society Abbott Laboratories, Abbott Park, Illinois
2000-2001	Manager of Conjugation Common Process and Associate Research Fellow, Volwiler Society Abbott Laboratories, Abbott Park, Illinois
2001-2004	Manager, Cancer Core R&D and Associate Research Fellow, Volwiler Society Abbott Laboratories, Abbott Park, Illinois

2004-Present Manager, Cancer Core R&D and Research Fellow, Volwiler Society Abbott Laboratories, Abbott Park, Illinois

PATENT APPLICATIONS AND SUPPORT

1. Provided scientific support for licensed technology patents from Wallac, OY, Turku, Finland on Assay of Free and Complexed Prostate-Specific Antigen, including technical support for successful defense of European Patent Opposition in Munich, March, 2003.

2. Dowell, B., King, C., Smith, A., and O'Morchoe, S. Immunoassys for Prostate Specific Antigen. Issued Febraury, 1997. Patent describes use of monoclonal antibody additive to monoclonal-polyclonal PSA assays to improve ability to detect free PSA and PSA-ACT complexes equally. WO 9518381 and US 5559677 This method is currently being used in Architect Total PSA assay.

3. Dowell, B., King, C., Smith, A., and O'Morchoe, S. Immunoassys for Prostate Specific Antigen. Issued September 30, 1997. Patent describes use of PSA-Free PSA antibody as a calibrator that mimics PSA-ACT. It also describes method of fractionating polyclonal antibodies into eptitopes that are masked by binding to PSA-ACT. US 5672480

3. Bridon, D., Dowell, B., Qiu, X, Petterrson, K., Piironen, T., Lilja, H. and Vihinen, M. Prostate Specific Peptides and Uses Thereof. US 6,143,509.

REGULATORY SUBMISSION SUPPORT

1. Member of PMA Submission Team for IMx AFP, which was first PMA supplement on IMx instrument. Efforts included presentation of IMx Instrument to FDA in Bethesda.

2. Member of 510K Submission Team for IMx PAP.

3. Member of PMA Submission Team for IMx PSA, which was first full PMA for cancer product on IMx. Efforts included presentation of performance characteristics and rare reagent characterization at FDA Panel Meeting.

4. Member of PMA Submission Team for AxSYM Free and Total PSA.

4. Supported French and Koseisho submissions for IMx AFP, IMx PAP, IMx CA15-3, AxSYM Free PSA, and AxSYM Total PSA.

5. Independent Reviewer for IMx Free and Total PMA submitted January 30, 2003 and approved in 2004.

TEST METHOD AND PROCESS VALIDATION SUPPORT

1. Project manager for AxSYM Free and Total PSA assays which were among first AxSYM assays to be fully validated, including primaries, rare reagents and list components under then current guidelines.

2. Manager for Conjugate Common Process, which covered PVA's for AP and HRPO periodate and forward and reverse heterobifunctional conjugation. Also covered test method for acridinium incorporation ratio and for % conjugation by GPC-HPLC.

ABBOTT COMMITTEES

1. ADD Cancer New Leads Assessment Committee, Manager
2. ADD Assay Standardization Committee

ABBOTT PUBLICATIONS

1. Perspectives on PSA. Abbott Diagnostics Educational Services, Technical Brochure, 1993.

2. Dowell, B., Schaefer, V., Crary A., and Weigand, R. Performance and clinical evaluation of AxSYM Free and Total PSA. Abbott PSA Monograph, Oscar Securado Editor., Abbott Diagnsotics Educational Services (Delkenheim), 1997, pages 9-13.

SELECTED ABBOTT SPONSORED PRESENTATIONS

1. Tumor Markers: An Overview. Oklahoma-Arkansas Bi-State Medical Technology Convention, Oklahoma City, OK, April 25, 1990.

2. Clinical Use and Development of Cancer Markers. William Beaumont Hospital Clinical Pathology Inservice, Royal Oak, MI. November 2, 1990.

3. Description and Utility of Available Tumor Markers. New Mexico State Society of American Medical Technologists 1991 Fall Meeting, Albuquerque, NM. September 28, 1991

4. The Biochemistry of PSA: A Complex Problem. Annual Scientific Symposium of Ontario Society of Clinical Chemists. North York, Ontario. November 3, 1993.

5. Cancer BU Experience with *E. coli* Alkaline Phosphatase (Discrepant Avoidance). ADD Technical Advisory Board Roundtable on Alkaline Phosphatase. Novmember 4, 1994.

6. PSA: Characteristics and Immunodetection. Annual Meeting of Private Laboratory Owners. San Juan, Puerto Rico, May 28, 1994.

7. Performance and Clinical Characteristics of Free and Total PSA. Clinical Investigators Meeting: Free PSA. European Urological Association, Paris, August, 1996.

8. Roundtable for Clinical Ligand Assay Society Annual Meeting. Use of Free PSA in Diagnosis of Prostate Cancer. March 24, 1997, Chicago, IL.

9. Abbott Day. Characteristics of AxSYM Free and Total PSA assays., Linx Austria, June 10, 1997,

10. Abbott Days. Utility of Free PSA and Characteristics of AxSYM Free and Total PSA assays. Maidenhead, England. June 18 and 19, 1997.

11. Member of Industry Roundtable for AACC Tumor Markers in Prostate Cancer Workshop, Chicago 2001, 2002 and 2003

12. Conjugation Common Process. For R&D, Operations and Quality, September, 2001.

13. Industry Rountable for Annual Meeting of Clinical Ligand Assay Society, Chicago, IL, May 2004. Guidelines for colorectal cancer screening

14. Tumor Marker Workshoop for Annual Meeting of Clinical Ligand Assay Society, Chicago, IL, May 2004.

BIBLIOGRAPHY

PUBLICATIONS

1. Dowell, B. L.: Properties of *in vitro* cultured Hodgkin's disease cells. Dissertation, June, 1977.

2. Robert, A. N., Smith, K. C., Dowell, B. L., and Hubbard, A. K.: Cultural, morphological, cell membrane, enzymatic and neoplastic properties of cell lines derived from a Hodgkin's disease lymph node. Cancer Res. 38: 3033-3043, 1978.

3. Dowell, B. L., Falletta, J. M., Moore, J. O., and Metzgar, R. S.: Detection and partial characterization of human thymus-leukemia antigens. J. Nat. Cancer Inst. 65:691-701, 1980.

4. Dowell, B. L., Segars, J. H., and Metzgar, R. S.: Physical separation of adenosine deaminase and a human thymus-leukemia antigen isolated from Molt 4. Cancer Res. 41:343-345, 1981.

5. Metzgar, R. S., Dowell, B. L., Lachman, L., Jones, N. H., and George, F. W. IV: Classification of human leukemia by membrane antigen analysis with xenoantisera. Cancer Res. 41:4781-4785, 1981.

6. Pullen, J., Falletta, J. M., Crist, W. M., Vogler, L. B., Dowell, B. L., Humphrey, G. B., Blackstock, R., van Eys, J., Cooper, M. D., Metzgar, R. S., and Meydrech, E. F.: Southwest Oncology Group experience with immunological phenotyping in acute lymphocytic leukemia of childhood. Cancer Res. 41:4802-4809, 1981.

7. Vogler, L. B., Crist, W., Sarrif, A., Pullen, J., Bartolucci, A., Falletta, J., Dowell, B., Humphrey, B. G., Blackstock, R., van Eys, J., Metzgar, R. S., and Cooper, M. D.: An analysis of clinical and laboratory features of acute lymphocytic leukemias with emphasis on 35 children with pre-B leukemia. Blood 58:135-140, 1981.

8. Metzgar, R. S., Borowitz, M., Jones, N. H., and Dowell, B. L.: The distribution of common ALL antigen (CALLA) in non-hematopoietic tissues. J. Exp. Med. 154:1249-1254, 1981.

9. Haynes, B. F., Dowell, B. L., Hensley, L. L., Gore, I., and Metzgar, R. S.: Reactivity of T cell monoclonal antibodies with primate lymphocytes. Science 215:298-300, 1982.

10. Dowell, B. L., Gore, I., Jr., McCormick, G. M., Haynes, B. F., and Metzgar, R. S.: A monoclonal antibody reactive with a second epitope of the 67,000-dalton human T cell antigen. Hum. Immunol. 7:95-104, 1983.

11. Pullen, D. J., Crist, W. M., Falletta, J. M., Boyett, J. M., Roper, M., Dowell, B., van Eys, J., Humphrey, G. B., Head, D., Brock, B. L., Blackstock, R., Metzgar, R. S., and Cooper, M. D.: A Pediatric Oncology Group classification protocol for acute lymphocytic leukemia (ALinC 13): Immunologic phenotypes and correlation with treatment results, in *Leukemia Research: Advances in Cell Biology and Treatment*, Eds. S. B. Murphy and J. R. Gilbert. Elsevier Science Publishing Co., Inc., 1983, pp. 221-239.

12. Falletta, J. M., Boyett, J., Pullen, D. J., Crist, W., Dowell, B., Roper, M., Humphrey, G. B., Metzgar, R., Cooper, M. D., and van Eys, J.: Clinical and phenotypic features of childhood acute lymphocytic leukemia by race and Spanish origin, in *Progress in Cancer .Research and Therapy, Volume 27, Pathogenesis of Leukemias and Lymphomas: Environmental Influences*, ed. I. T. Magrath, G. T. O'Connor, and B. Ramot. Raven Press, New York, 1984, pp. 191-195.

13. Dowell, B. L., Tuck, F. L., Borowitz, M. J., LeBien, T. W., and Metzgar, R. S.: Phylogenetic distribution of a 24,000 dalton human leukemia-associated antigen on platelets. and kidney cells. Comparative and Develop. Immunol. 8:187-195, 1984.

14. Pullen, D. J., Boyett, J. M., Crist, W. M., Falletta, J. M., Roper, M., Dowell, B., van Eys, J., Jackson, J. F., Humphrey, G. B., Metzgar, R. S., and Cooper, M. D.: Pediatric Oncology Group utilization of immunologic markers in the designation of acute lymphocytic leukemia subgroups: Influence on treatment response. Ann. N. Y. Acad. Sci. 428:29-48, 1984.

15. Borowitz, M. J., Dowell, B. L., Boyett, J. M., Falletta, J. M., Pullen, J., Crist, W. M., Humphrey, G. B., and Metzgar, R. S.: Monoclonal antibody definition of T-cell acute leukemia. A Pediatric Oncology Group Study. Blood 65:785-788, 1985.

16. Crist, W., Pullen, J., Boyett, J., Falletta, J., van Eys, J., Borowitz, M., Jackson, J., Dowell, B., Frankel, L., Quddus, F., Ragab, A., and Vietti, T.: Clinical and biologic features predict poor prognosis in acute lymphoid leukemias in infants: A Pediatric Oncology Group study. Blood 67:135-140, 1986.

17. Borowitz, M. J., Dowell, B. L., Boyett, J. M., Pullen, D. J., Crist, W. M., Quddus, F. M., Falletta, J. M., and Metzgar, R. S.: Clinicopathologic aspects of E rosette negative T cell acute lymphoblastic leukemia. A Pediatric Oncology Group study. J. Clin. Oncol. 4:170-177, 1986.

18. Freeman, J. W., Dowell, B. L., Ochs, R. L., Ross, B. E., and Busch, H.: Effect of differentiation on the expression of a nucleolar antigen with a molecular weight of 145,000 in HL-60 cells. Cancer Res. 47:586-591, 1987.

19. Dowell, B. L., Borowitz, M. J., Boyett, J. M., Pullen, D. J., Crist, W. M., Quddus, F. F., Russell, E. C., Falletta, J. M., and Metzgar, R. S.: Immmunologic and clinicopathologic features of common acute lymphoblastic leukemia antigen (CALLA)-positive childhood T cell leukemia. A Pediatric Oncology Group study. Cancer 59:2020-2026, 1987.

20. Crist, W., Pullen, J., Boyett, J., Falletta, J., van Eys, J., Borowitz, M., Jackson, J., Dowell, B., Russell, C., Quddus, F., Ragab, A., and Vietti, T.: Acute lymphoid leukemia in adolescents: Clinical and biologic features predict a poor prognosis. A Pediatric Oncology Group Study. J. Clin. Oncology 6:34-43, 1988.

21. Shuster, J. J., Falleta, J. M., Pullen, J., Crist, W. M., Humphrey, G. B., Dowell, B. L., Wharam, M. D., and Borowitz, M. Prognostic factors in childhood T-cell acute lymphoblastic leukemia: a Pediatric Oncology Group study. Blood. 75:166-173, 1990.

22. King, W. J., Tomita, J. T., and Dowell, B. L. Strategies for heterogeneous enzyme immunoassays for tumor markers. In *Immunodiagnosis of Cancer, 2nd Edition.* R. B. Herberman and D. W. Mercer, Editiors. Marcel Dekker, Inc., New York, pp 83-94, 1990.

23. Dreyer, Z.E., Dowell, B.L., Chen H., Hawkins, E., and McClain, K.L. Infection-associated Hemophagocytic Syndrome. Evidence for Epstein-Barr Virus Gene Expression. Amer. J. Ped. Hematol. Oncol. 13:476-481, 1991.

24. Bridon, D.P. and Dowell, B.L. Structural Comparison of prostatic specific antigen (PSA) and human glandular kallikrein (hK2) using molecular modeling. Urology, 45:801-806, 1995.

25. Oesterling, J.E., Jacobsen, S.J., Klee, G.G., Pettersson, K., Piironen, T., Abrahamsson, P-A., Stenman, U-H, Dowell, B., Lovgren, T, and Lilja, H. Free, complexed, and total serum PSA: The establishment of appropriate reference ranges for their concentration and ratios. J. Urology 154:1090-1095, 1995.

26. Zhang, W-M, Leinonen, J., Kalkkinen, N., Dowell, B., and Stenman, U-H., Purification and characterization of different molecular forms of prostate specific antigen in human seminal fluid. Clin. Chem, 41: 1567-1573, 1995.

27. Lovgren, J, Piironen, T, Overmo, C., Dowell, B., Karp, M., Pettersson, K, Lilja, H., and Lundwall, A. Production of recombinant PSA and HK2 and analysis of their immunological cross reactivity. Biochem. Biophys. Res. Commun. 213:888-895, 1995.

28. Piironen, T, Lovgren, J, Karp, M, Eerola, R, Dowell, B, Lovgren, T, Lilja, H, and Petterrson, K. A novel immunofluorometric sandwich assay for the measurement of glandular kallikrein (hK2) from serum. Clin. Chem, 42:1034-1041, 1996.

29. Eerola, R, Piironen, T, Pettersson, K, Lovgren, J, Vehniainen, Lilja, H, Dowell, B., Lovgren, T. and Matti, K. Immunoreactivity of recombinant human glandular kallikrein using monoclonal antibodies raised against prostate specific antigen. Prostate, 31:84-90, 1997.

30. Dowell, B., Jacobson L., Friese, J., Rapp, J., Miceli, C., Loewen, N., Lauren, L., Salle, J., Slota, J., Segurado, O., and Weigand, R. Development of the Abbott AxSYM Free PSA assay. Performance characteristics and preliminay clinical evaluation. Anticancer Res., 17:3037-3078, 1997.

31. Segurado O. G., Volmer, W., and Dowell, B. L. PSA standardization: a review of NCCLS, Stanford and Abbott efforts. Anticancer Res. 17:2919-2920, 1997.

32. NCCLS Subcommitee for PSA Standadization. NCCLS I/LA19-A: Primary reference preparations used to standardize calibration of immunochemical assays for serum prostate specific antigen (PSA), Approved guideline (1977).

33. Vashi A. R., Wojno, K. J., Henricks, W., England, B. A., Vessella R. L., Lange, P. H., Wright Jr., G. L., Schellhammer, P. F., Weigand R. A., Olson R. M., Dowell, B. L., Borden, K. K., Oesterling J. E., Determination of the "reflex range" and appropriate cutpoints for percent free prostate-specific antigen in 413 men referred for prostatic evaluation using the AxSYM system. Urology 4(:19-27, 1997.

34. Piironen, T., Villoutreix B., Becker, C., Hollingsworth K., Vihinen, M., Bridon, D., Qiu X., Rapp, J., Dowell, B., Lovgren, T., Pettersson, K., and Lilja, H. Determeination and analysis of prostate specific antigen (PSA) and human glandular kallikrein (hK2) antigenic epitopes using synthetic peptides and computer modeling. Protein Sci. 7:259-269, 1998.

35. Stenman, UH. et. al. Summary report of the TD-3 Workshop: Characterization of 83 antibodies against prostate-specific antigen. Tumor Biol. 20 (Suppl. 1): 1-13, 1999.

36. Slota, J., Lauren, L., Rapp, J., and Dowell, B.L. Immunological grouping of 53 antibodies against prostate-specific antigen. Tumor Biol. 20 (Suppl. 1):70-74, 1999.

37. Leinonen, J., Leinimaa, M., Zhang, W.-M., Piironen, T., Pettersson, K., Lilja, H., Dowell, B., and Stenman, U-H. Reactivity of anti-PSA monoclonal antibodies with recombinant human kallikrein-2. Tumor Biol. 20 (Suppl. 1):35-37, 1999.

38. Nustad K., Dowell B. L., Davis, G. J., Stewart, K., Nilsson, O., Roijer, E. Suminami, Y., Nawata, S., Cataltepe, S., Silverman, G.A., Kato, H., and de Bruijn, H.W.A., Characterization of monoclonal antibodies directed agaist sqaumous cell carcinoma antigens. Report of the TD-10 Workshop. Tumor Biology 25 (1-2), 69-90,2004

39. Moller Sorensen N, Dowell, BL, Stewart KD, Jensen V, Larsen L. Lademann U, Murphey G, Nielsen HJ, Brunner N. and Davis G. Establishment and characterization of 7 new monoclonal antibodies to tissue inhibitor of metalloprotienases-1. Tumor Biology 26(2), 71-89, 2005..

ABSTRACTS

I. Roberts, A. N., Page, R. C., and Dowell, B. L.: Specificity of transfer factor from lymphocytes sensitized *in vitro* with melanoma antigen extract. Proc. American Association for Cancer Research, San Diego, California, May 7-11, 1975.

2. Dowell, B. L., Roberts, A. N., and Smith, K. L.: Properties of *in vitro* cultured Hodgkin's disease cells. Bacteriol. Proc. 76:66, l976.

3. Dowell, B. L., and Metzgar, R. S.: Detection of a human thymus-leukemia antigen by monkey antisera to human thymocytes. Fed. Proc. 38:1461, l979.

4. Gordon, D. S., Vogler, W. R., Byrnes, R. K., Meyer, L. M., Dowell, B. L., and Metzgar, R. S.: Immunological characterization of adult acute undifferentiated leukemia. Proc. American Society of Clinical Oncology, Washington, D. C., April 30-May 2, l981.

5. Dowell, B. L., and Metzgar, R. S.: Further characterization of human thymus-leukemia antigen, *in* Advances in Comparative Leukemia Research 1981, ed. D. S. Yohn and J. R. Blakeslee. Elsevier, New York, pp. 511-512, 1981.

6. Metzgar, R. S., Borowitz, M., Jones, N. H., and Dowell, B. L.: The distri- bution of common ALL antigen (CALLA) in non-hematopoietic tissues, *in* Advances in Comparative Leukemia Research 1981, ed. D. S. Yohn and J. R. Blakeslee. Elsevier, New York, pp. 525-527, 1981.

7. Dowell, B. L., Gore, I. Jr., McCormick, G. M., and Metzgar, R. S.: Monoclonal antibodies against the T-cell chronic lymphocytic leukemia- derived cell line, SKW3. Fed. Proc. 4l:270, l982.

8. Quddus, F. F., Kaufmann, S. H., Roper, M., Dowell, B., Pullen, J., Leventhal, B. G.: Glucocorticoid receptor (GB) level in pediatric leukemia cells. Proc. American Society of Clinical Oncology, St. Louis, Missouri, April 28-May 1, 1982.

9. Boyett, J., Pullen, J., Crist, W., van Eys, J., Berry, D., Leventhal, B., Kim, T., Ravindranath, Y., Dowell, B., and Roper, M.: Immune phenotype is an independent prognostic factor within non-T, non-B acute lymphocytic leukemia (ALL): Initial WBC is not prognostic within pre-B ALL. Proc. American Society of Hematology, San Antonio, Texas, December 5-8, l982.

10. Dowell, B. L., and Mukhopadhyay, N.: A possible prognostic value of mitogenic responses in non-T, non-B childhood acute lymphocytic leukemia (ALL). Proc. Southwest Section, American Association for Cancer Research, New Orleans, Louisiana, October 27-28, 1983.

11. Pullen, J., Crist, W., Boyett, J., Falletta, J., van Eys, J., Borowitz, M., Jackson, J., Dowell, B., Russell, C., Quddus, F., Ragab, A., and Vietti, T.: Clinical and biologic features predict poor prognosis in adolescent acute lymphocytic leukemia (ALL). Proceedings of the American Society of Clinical Oncology, Toronto, Ontario, May 6-8, 1984.

12. Borowitz, M. J., Boyett, J. M., Dowell, B. L., Pullen, D. J., Metzgar, R.S., Humphrey, G. B., van Eys, J., and Falletta, J. M.: Clinicopathologic aspects of E rosette negative T cell acute lymphoblastic leukemia (T-ALL). Proc. American Society of Clinical Oncology, Toronto, May 6-8, 1984.

13. Dowell, B. L., and Mukhopadhyay, N.: Prognostic value of mitogenic responses in non-T, non-B childhood acute lymphocytic leukemia (ALL). Proc. American Association for Cancer Research, Toronto, May 9-12, 1984.

14. Dowell, B. L., Boyett, J. M., Borowitz, M. J., Falletta, J. M., Pullen, D. J., Crist, W. M., van Eys, J., Metzgar, R. S., Starling, K. A., and Humphrey, G. B.: Immunologic and clinicopathologic features of common acute lymphocytic leukemia antigen (CALLA)-positive, T cell leukemia. Proc. American Association for Cancer Research, Toronto, May 9-12, 1984.

15. Humphrey G. B., Boyett, J., Dowell, B., Kim, T. H., Crist, W., Richie, E., Griffith, R., Blackstock, R., and Newberg, R.: Complement receptor positive (C'R+) acute lymphocytic leukemia (ALL) is unevenly distributed among the B and T lineage phenotypes of ALL & appears to lack distinguishing clinical features or independent prognostic significance. Proc. American Association for Clinical Research, Toronto, May 9-12, 1984.

16. Crist, W., Pullen, J., Boyett, J., Falletta, J., van Eys, J., Borowitz, M., Jackson, J., Dowell, B., Frankel, L., Quddus, F., Ragab, A., and Vietti, T.: Clinical and biologic features predict poor prognosis in acute lymphocytic leukemia (ALL) in infants. Proc. International Society of Pediatric Oncology (SIOP), Barcelona, September 17-21, 1984.

17. Weiner, M., Borowitz, M., Boyett, J., Civin, K., Metzgar, R., McKolnis, J., Crist, W., Dowell, B., and Pullen, J.: Clinical pathologic aspects of myeloid antigen positivity in pediatric patients with acute lymphoblastic leukemia (ALL). Proc. American Society of Clinical Oncology, Houston, May 19-21, 1985.

18. Pullen, J., Crist, W., Boyett, J., Falletta, J., van Eys, J., Borowitz, M., Jackson, J., Dowell, B., Frankel, L., Quddus, F., Ragab, A., and Vietti, T.: Infants have biologically different and clinically more aggressive acute leukemia (ALL) than older children. Proc. American Society of Clinical Oncology, Houston, May 19-21, 1985.

19. Dowell, B. L., Mahoney, D. H., Steuber, C. P., Starling, K. A., and Fernbach, D. J.: Level of circulating T cells in non-T, non-B acute lymphoblastic leukemia (ALL) of childhood: A prognostic factor. Proc. American Association for Cancer Research, Houston, May 22-25, 1985.

20. Dowell, B. L., and Fernbach, D. J.: Immunophenotyping of seventy-one cases of childhood acute lymphoblastic leukemia (ALL) of the non-T, non-B type. Proc. American Society of Hematology, New Orleans, December 7-10, 1985.

21. Freeman, J. W., Dowell, B., Ochs, R., and Busch, H.: A cell cycle specific nucleolar antigen (p145). Proc. American Association for Cancer Research, Los Angeles, May 7-10, 1986.

22. Dowell, B., Mahoney, D., Steuber, C., Starling, K., and Fernbach, D.: Level of circulating T cells in non-T, non-B acute lymphoblastic leukemia (ALL) of childhood: A prognostic factor. Proc. Clinical Immunology Society, Baltimore, October 10-12, 1986.

23. Pullen, J., Boyett, J., Borowitz, M., Dowell, B., Falletta, J., Krejmas, N., Sexauer, C., and Crist, W.: How important is common acute lymphocytic leukemia antigen (CALLA) negativity as a prognostic factor in children excluding infants with B-precursor acute lymphocytic leukemia (ALL)? Proc. American Society of Clinical Oncology, May 17-19, 1987.

24. Dowell, B. L., Mahoney D. H., Steuber, C. P., Fernbach, D. J. Immunophenotypic changes in children with acute lymphoblastic leukemia (ALL) at relapse. Leukemia Society of America, March, 1987.

25. Dowell, B., Bryg, K., Wikstrom, K., Beykirch, K., Rapp, J., and Shaw, N. A new IMx™ automated microparticle ensyme immunoassay for the quantiation of human alpha-fetoprotein. Clin. Chem. 34:1161 , 1988.

26. Rightmire, Z., Dowell, B., and McClain, K. Expression of Epstein-Barr virus genes in tissues of patients with the infection-associated hemophagocytic syndrome. Proc. Amer. Assoc. Cancer Res., 1988.

27. Dreyer, Z., Dowell, B., and McClain, K. Role of Epstein-Barr virus gene expression in histiocytic activation. Soc. for Leukocyte Biol., October, 1988.

28. Dowell, B. L., Bairstow, C. S., Hutton, J. M. and Sanders, J. R. Maternal Serum Alpha-Fetoprotein Testing: A Partnership. Newsletter of Clin. and Diag. Immunol. Div., Amer Assoc. Clin. Chem., 4:9,13, 1989.

29. Dowell, B., Borden, K., and Shaw, N. IMx™ AFP, an automated miroparticle immunoassay for alpha-fetoprotein (AFP): Performance characteristics and clinical studies. Clin. Chem., 35:1192, 1989.

30. Dowell, B., Borden, K., Hutton, J. and Shaw, N. IMx™ AFP: An Automated Microparticle Immunoassay for Alpha-Fetoprotein (AFP): Performance characteristics and clinical studies. Newsletter of Clin. and Diag. Immunol. Div., Amer Assoc. Clin. Chem., 3: 24-25, 1989.

31. Hutton, J., Borden, K., Porter, G., Dowell, B., Rapp, J., Shaw, N., Lennartz, L., Vendely, P., Pham, T., Ebert, W., and Daver, A. Performance characteristics and clinical evaluation of the Abbott IMxc SCC. Clin. Chem. 36: 1060, 1990.

32. Schaefer, V., Dowell, B., Borden, K., Wright, G.L. Jr., Chan, D.W., Lange, P.H., Vessella, R.L., Bates, H.A., and Fritsche, H.A. Multi-site clinical study of the IMx PSA assay. Presented October, 1991. XIX Annual Meeting of the International Society of Oncodevelopmental Biology and Medicine, Sienna, Italy.

33. Rozzell, M., Morningstar, M., Schaefer, V., Dowell, B., Schellhammer, P., and Wright, G. Jr. Clinical trial of Abbott IMx PSA, an enzyme immunoassay for the quantitation of prostate specific antigen in human serum. American Cancer Society, Virginia Division, 1992.

34. Schaefer, V., Borden, K., Friese, J., Alexander, D., Dowell, B., Wright, G., Morningstar, M., Vessella, R., and Close, B. Multi-site clinical study of the IMx PAP assay. Clin. Chem. 39:1188, 1993.

35. King, C., Friese, J., Lauren, L., Dowell, B., Shaw, N., Lilja, H., Stenman, U-H., Piironen, T., and Pettersson, K. Measurement on the IMx Immunoassay System of free and total forms of prostate specific antigen for differentiation of patients with benign prostatic hyperplasia and prostate cancer. Presented at Annual Meeting Amer. Assoc. Clin. Chem. 1994.

36. Lilja, H., Bjork, T., Abrahamsson, P-A., Stenman, U-H., Shaw, N., Dowell, B., Oesterling, J., Pettersson, K., Piironen, T., and Lovgren, T. Improved separation between normals, benign prostatic hyperplasia, and carcinoma of the prostate by

measuring free, complexed and total concentrations of prostate specific antigen. J. Urology 151:400A, 1994.

37. Osterling, J., Jacobsen, S., Klee, G., Pettersson, K., Piironen, T., Stenman, U-H., Lovgreen, T., Dowell, B., Abrahamsson, P-A., and Lilja, H. Free, complexed, and total serum PSA: Establishment of age-specific reference ranges using newly developed immunofluorometric assays (IFMA). J. Urology 151:311A, 1994.

38. Slota, J., Prine, B, Magic, S., Dowell, B., and Huhn, O. Detection of a circulating immune complex of PSA and IgG in a patient with benign prostatic hyperplasia and hypergammaglobulinemia. Presented at XXII Meeting of International Society for Oncodevelopmental Biology and Medicine, Groningen, The Netherlands, September, 1994.

39. Dowell, B., King, C. , Weatherholt, J., and Schaefer, V. Differential recognition of PSA forms is not reflected in the clinical performance of IMx PSA. Presented at XXII Meeting of International Society for Oncodevelopmental Biology and Medicine, Groningen, The Netherlands, September, 1994.

40. Krikau, M, Dowell, B., Jacobson, L., Kasen, L., Moolji, N., Rapp, J., Rupprecht, J., Wikstrom, K., Shaw, N., and Wilson, G. A new IMx automated enzyme immunoassay for the quantitative measurement of CA15-3 assay values in human serum and plasma. Presented at XXII Meeting of International Society for Oncodevelopmental Biology and Medicine, Groningen, The Netherlands, September, 1994.

41. Dowell, B., Friese, J., Dunlop, C., Booker, M., Weigand, R. and Barnes, W. Free\Total PSA Ratios in an Early Detection Study. Presented June, 1995 to XXIII Meeting of International Society for Oncodevelopmental Biology and Medicine.

42. Dowell, B., Jacobson, L., Friese, J., Rapp, J., Miceli, C., Loewen, N., Lauren, L., Salle, J., Moolji, N., Booker, M., Dunlop, C., Williams, R., Stein, L., Harker, K., Wachholz, J., Barnes, W., Slota, J., Ruffalo, J., Weigand, R. Development of Abbott AxSYM Total PSA and Free PSA Assays. Presented Sept, 1995 to XXIII Meeting of International Society for Oncodevelopmental Biology and Medicine.

43. Qiu, X., Bridon, D., Dowell, B. and Stewart, K. Molecular modeling of PSA, hGK-1 and PSA-ACT Complex. Abstracts of Papers of the Amer. Chem. Soc. 210: 1995.

44. Slota, J., Lauren, J., Rapp, J., and Dowell, B. Immunological subgrouping of ISOBM PSA Workshop Antibodies. Presented Sept, 1995 to XXIII Meeting of International Society for Oncodevelopmental Biology and Medicine.

45. Pettersson, K., Piironen, T., Lovgren, J., Karp, M., Lovgren, T, Dowell, B., and Lilja, H. Sensitive immunoassay for the specific detection of human glandular kallikrein 2 (hK2). Presented Sept, 1995 to XXIII Meeting of International Society for Oncodevelopmental Biology and Medicine.

46. Segurado, O., Vollmer, W., and Dowell, B. PSA standardization: A review of NCCLS, Stanford, and Abbott efforts. Submitted to Hamburger Symposium uber Tumormarker, October 1995.

47. Dowell, B., Jacobson, L. Friese, J., Rapp, J., Miceli, C., Loewen, N., Lauren, L., Salle, J., Slota, J., Seguragdo, O., and Weigand, R. Development of the Abbott AxSYM Free PSA assay: Performance characteristics and preliminary clinical evaluation. Presented at Hamburger Symposium uber Tumormarker, October, 1995.

48. Pettersson, K., Piironen, T., Lovgren, J., Karp, M., Lovgren, T., Dowell, B. and Lilja, H. Novel, specific and sensitive immunoassay for hK2 mesures low concentrations of serum hK2 compared to PSA. Proceedings of American Urological Association, J Urology 155:695A, 1996.

49. Corey, E., Wegner, S.K., Stray, J. E., Corey, M. J., Arfman, E. W., Vesella, R. L., and Dowell, B. L. Physical characterization of prostate-specific antigen (PSA) epitopes using complementary immunochemical techniques. Proceedings of American Urological Association, J Urology 155:697A, 1996.

50. Oesterling, J. E., Wojno, K. J., Vessella, R. L., Lange, P. H., Noteboom, J., Wright, G. L. Jr., Schellhammer, P. F., Weigand, R. A. , Olson, R. M., Dowell, B. L. A comparison of free to total PSA (F/T) ratio to total PSA for distinguishing benign prostatic hyperplasia (BPH) from prostate cancer (CaP) using the Abbott AxSYM system. Proceedings of American Urological Association, J Urology 155:370A, 1996.

51. Dowell, B., Friese, J., Rapp, J., Miceli, C., Loewen, N., Lauren, L., Salle, J., Slotta, J., Dunlop, C., and Weigand, R. Development of the Abbott AxSYM Total PSA and Free PSA assays: Performance characteristics and preliminary clinical evaluation. Clin. Chem. 42: 705, 1996.

52. Dowell, B., Friese, J., Dunlop, C., Booker, M., Weigand R., Barnes, W., Gladrow, E. Free/Total PSA ratios in an early detection study. Klinisches Labor 42:521-523, 1996.

53. Dowell, B., Jacobson, L. Friese, J., Rapp, J., Miceli, C., Lauren, L., Salle, J., Moolji, N., Booker, M., Dunlop C., Williams, R., Stein., L., Wachhloz, J., Barnes, W., Slota, J., Ruffalo, J., Weigand, R., Gladrow, E. Development of the AxSYM Total PSA and Free PSA assays for the Abbott AxSYM instrument. Klinisches Labor, 42: 525-526, 1996.

54. . Piironen, T., Lovgren, J., Karp, M., Lovgren, T, Dowell, B., Lilja, H, and Pettersson, K. A novel immunoassay for the specific measurement of prostatic human glandular kallikrein 2 (hK2) in serum. XVI IFCC Meeting, 1996.

55. Rapp, J., Salle, J., Dowell, B., and Weigand, R. Use of the Stanford 90:10 reference PSA to standardize the AxSYM Free and Total PSA Assays. ISOBM, November 1996.

56. Dowell, B., Munoz, J., and Weigand, R. Multi-assay comparison of AxSYM Total PSA assay using serum samples and the Stanford 90:10 PSA Standard. ISOBM Meeting, Montreaux, Switzerland, September, 1997.

57. Piironen, T., Pettersson, K., Vihinen, M., Lovgren, T., Dowell, B., Bridon, D., Villotreix, B., and Lilja, H. Determination of prostate specific antigen (PSA) and human glandular kallikrein (hK2) epitopes by synthetic peptides. Amer Urol Soc Meeting, New Orleans, LA, April, 1997.

58. Piironen, T., Villotreiz B.O., Becker C., Hollingsworth, K., Vihinen, M., Bridon, D., Qiu, X. Rapp, J., Dowell, B., Lovgren, T., Pettersson, K., and Lilja, H. Analysis of antigenic epitopes of prostate specific antigen (PSA) and human glandular Kallikrein (hK2) using synthetic peptides and computer modeling. ISOBM Meeting, Montreaux, Switzerland, September, 1997.

59. Segurado OG, Dowell B, Schaefer V, Crary A, and Weigand R. Two Cut-off points and a reflex range enhance the clinical utility of Abbott Total and Free PSA. ISOBM Meeting, Montreaux, Switzerland, September, 1997.

60. Dowell, B. L, Vessella, R., Partin, A., Wojno, K., Sasse, E., Moul, J, Woolf, P., Wong, P. Y., Crawford, E. D., Wright, G. L. Jr., Schaefer, V. C., and Weigand, R. A. Estimation of cancer probabilities using AxSYM Free and Total assays and digital rectal examination (DRE). Tumor Biol 19 (S2):66, 1998.

61. Friese, J., Dowell, B., Schaefer, V., Vessella R., Borden, K. Wright, G. Jr., Woolf, P., Sasse, E., and Weigand R. A. Age-specific reference ranges for IMx Free PSA and Total PSA assays. Tumor Biol 19 (S2):66, 1998.

62. Frise J, Lipowsky C, Song M, Xu M, Sinio L, Stein L, William R, Dowell B and Weigand R. Total PSA determination using the IMx Total PSA assay. Clin. Chem. 44 (6 Supplement), 1988.

63. Dowell, B. L., Borden, K., Schaefer, V., Crary A., Vessella, R., Wright, G. Jr., Woofl, P., Sasse, E. and Weigand, R. Age-specific reference ranges for AxSYM Free PSA and AxSYM Total PSA assays. AACC Meeting, 1998.

64. Piironen, T., Villoutreix, B. O., Becker, C., Hollingsworth, K., Vihinen, M., Bridon, D., Qiu, X., Rapp, J., Dowell, B., Lovgren, T., Pettersson, K., and Lilja, H. Analysis of antigenic epitopes of prostate specific antigen (PSA) and human glandular kallikrein (hK2) using synthetic peptides and computer modeling. XII Congress, European Assoc. Urology, Bacelona, Spain, March, 1998.

65. Dowell, B, Kiefer, C., May, M., Bishop, J., Sequeria, A., Asmus, C., Lipowsky, C., Cooper, M., Pearlman, S., *et al.* Performance characteristics of the AxSYM DPD assay. Clin Chem Lab Med 37: Special Supplement, S429, 1999.

66. Dowell B, Vessella R, Schaefer V, and Petredies V. Free and Total PSA Stability. Presented at ISOBM Meeting, Barcelona, October 2001.

67. Schaefer, V., Petrides, v., Vessella, R., Wright, G. Chan, D., and Dowell, B. Age-specific reference ranges for the ARCHITECT Total PSA assay. Accepted for presentation at IFCC Meeting, Barcelona, 2003.

68. Davis, G. and Dowell, B. Epitope Mapping of Antibodies from ISOBM Squamous Cell Antigen Workshop. ISOBM Meeting, Edinburg, Scotland, August, 2003.

69. Davis, G, Salle, J, and Dowell, B. Pre-analytical studies of plasma TIMP-1 quantitation. ISOBM Meeting, Edinburg, Scotland, August, 2003

70. Davis, G., Sorensen, N., Stewart, K., Salle, J., Olson, J., Brunner, N., and Dowell, B. Characterization of monoclonal antibodies to human tissue inhibitor of metalloproteinase-1 (TIMP-1) and modeling of TIMP-1 and Matrix Metalloproteinase (MMP) Interactions. Submitted to Clinical Ligand Assay Society, May 2004, Chicago.

71. Sorensen, N. M., Jensen, V., Lademann, U., Dowell, B., Nielsen H. J., Brunner, N., and Davis, G., Establishmen and characterization of 8 new TIMP-1 monclonal antibodies. Submitted to ISOBM, June 2004, Helsinki, Finland.